Genomic Profiling of BDE-47 Effects on Human Placental Cytotrophoblasts.

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Public Summary:
Despite gradual legislative efforts to phase out flame retardants (FRs) from the marketplace, polybrominated diphenyl ethers (PBDEs) are still widely detected in human maternal and fetal tissues, eg, placenta, due to their continued global application in consumer goods and inherent biological persistence. Recent studies in rodents and human placental cell lines suggest that PBDEs directly cause placental toxicity. During pregnancy, trophoblasts play key roles in uterine invasion, vascular remodeling, and anchoring of the placenta-fetal unit to the mother. Thus, to study the potential consequences of PBDE exposures on human placental development, we used an in vitro model: primary villous cytotrophoblasts (CTBs). Following exposures, the endpoints that were evaluated included cytotoxicity, function (migration, invasion), the transcriptome, and the methylome. In a concentration-dependent manner, common PBDE congeners, BDE-47 and -99, significantly reduced cell viability and increased death. Upon exposures to sub-cytotoxic concentrations (</= 5 microM), we observed BDE-47 accumulation in CTBs with limited evidence of metabolism. At a functional level, BDE-47 hindered the ability of CTBs to migrate and invade. Transcriptomic analyses of BDE-47 effects suggested concentration-dependent changes in gene expression, involving stress pathways, eg, inflammation and lipid/cholesterol metabolism as well as processes underlying trophoblast fate, eg, differentiation, migration, and vascular morphogenesis. In parallel assessments, BDE-47 induced low-level global increases in methylation of CpG islands, including a subset that were proximal to genes with roles in cell adhesion/migration. Thus, using a primary human CTB model, we showed that PBDEs induced alterations at cellular and molecular levels, which could adversely impact placental development.

Scientific Abstract:
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